PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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CANADA

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.11.2004
Applicant's or agent's file reference *	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA 03/01372	16.09.2003	16.09.2002

Applicant
JOULE MICROSYSTEMS CANADA INC. et Al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Rasmussen, S Tel. +31 70 340-4595

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference *	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA 03/01372	International filing date *(day/month/year)* 16.09.2003	Priority date *(day/month/year)* 16.09.2002
International Patent Classification (IPC) or both national classification and IPC A61B5/00		
Applicant JOULE MICROSYSTEMS CANADA INC. et Al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15.04.2004	23.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Knüpling, M Telephone No. +31 70 340-2891

Re Item IV

Lack of unity of invention

1. This Authority considers that there are 2 inventions covered by the claims indicated as follows:

   I: Claims 1 - 6 directed to an optical system comprising digital signal processing control means and its use;

   II. Claims 7 - 14 directed to a method for generating reflectance and fluorescence characteristics.

2. The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

2.1 Document D5 is considered as representing prior art.
With respect to this document, claim 1 additionally discloses (see also item V below):

> a digital signal processing means for controlling the functionality of the photonic energy source, the optical emission processing means, and the received light optical processing means.

This feature is considered as a special technical feature of the first set of claims. It solves the problem of how to improve controlling of the device.

2.2 With regard to the second set of claims, the difference between claim 7 and D5 is the step of:

> collecting and correlating encoded fluorescence from the tissue; and repeating steps a) through e) for a next one or more wavelengths of electromagnetic radiation.

These features solve the problem of how to extract additional information (related to fluorescence properties of the tissue) from the tissue.

2.3 The special technical features of the two sets of claims are different. They are also not corresponding since they solve different technical problems. Consequently, it is concluded that the two sets of claims are not so linked as to form a single

inventive concept, contrary to Rule 13.1 and 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The amendments filed with the International Bureau under Article 19(1) introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 19(2) PCT. The amendments concerned are the following:

1.1 New claims 1 and 6 comprise the feature of 'encoding by pseudo random codewords'. The application as originally filed only disclosed 'binary pulse coding'.

1.2 New claims 12 - 14 introduce features ('statistical significance, 'comparative pattern') which have no basis in the original application.

1.3 Consequently, the amendments introduce new subject-matter.

In the following assessment of novelty and/or inventive step, the unallowable amendment will be ignored.

2. Reference is made to the following documents:

D3: US-A-5 303 026 (STROBL KARLHEINZ ET AL) 12 April 1994 (1994-04-12)
D5: US-B-6 345 194 (Nelson Robert S) 05-02-2002 (2 February 2002)
D6: WO-A-01 40776 (Wilson David A.) 07-06-2001 (7 June 2001)

The documents D5 and D6 were not cited in the international search report. Copies of the documents are appended hereto.

3. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 and 6 do not involve an inventive step in the sense of Article 33(3) PCT.

3.1 The document D5 is regarded as being the closest prior art to the subject-matter of claim 1 and discloses (the references in parentheses applying to this document):

An optical system for detecting one or more optical responses of biological tissue, said optical system comprising:
(a) a photonic energy source for emitting electromagnetic radiation (col. 10, l. 45 - 47) ;
(b) an optical emission processing means for receiving the electromagnetic radiation from the photonic energy source and isolating one or more illumination wavelengths of the electromagnetic radiation, said optical emission processing means encoding the one or more illumination wavelengths using one or more pseudo random codewords or linear FM thereby generating an encoded signal, the optical emission processing means transmitting the encoded signal to the biological tissue (col. 10, l. 47 - 67, where 'chirp pulses' are considered as linear FM encoding);
(c) an optics assembly providing a means for aligning emitter optics of the optical emission processing means with detector optics of a received light optical processing means (col. 8, l. 57 - 62);
(d) a received light optical processing means for collecting and isolating one or more wavelengths of received electromagnetic radiation from the biological tissue created in response to the encoded signal and transmitting the one or more wavelengths of received electromagnetic radiation to an optical detector (col. 8, l. 57 - 62);
(e) an optical detector for sensing and converting the one or more wavelengths of received electromagnetic radiation into an electrical signal (col. 8, l. 53 - 57); and
(f) digital signal processing means for correlating the electrical signal received from the optical detector with the encoded signal thereby identifying an optical response of the biological tissue to the one or more illumination wavelengths (col. 8, l. 51 - 53; col. 10, l. 58 - col. 11, l. 3).

3.2 The subject-matter of claim 1 therefore differs from this known device in the following feature:

a digital signal processing means for controlling the functionality of the photonic energy source, the optical emission processing means, and the received light optical processing means.

3.3 However, spectrometers as disclosed in D5 are usually computer controlled and it would be an obvious design measure for the man skilled in the art to implement a

computer control into a the device according to D5.

4. With regard to independent claim 6, reference is made to D3.

4.1 D3 discloses all features of claim 6 (col. 5, l. 42 - 45, optical fiber 18, spectrum analyzer 20, computer 24) except for the following features:

I. a digital signal processing means for controlling the functionality of the photonic energy source, the optical emission processing means, and the received light optical processing means;

II. coding the illumination using random codewords or linear FM and correlating the detector signal with the encoded signal.

4.2 With respect to feature I reference is made to section 3.3 above. Computer control is standard in modern spectrometers and it would be obvious for the man skilled in the art to implement computer control in a spectrometer already known from D3.

4.3 With respect to feature II, the effect of this difference is that noise which is not coded, is filtered out. The underlying problem can thus be formulated as how to reduce noise. The problem of noise entering the system is already acknowledged in D3 in column 3, l. 4 - 10. Here, the solution proposed is pulsing the light source the reduce exposure time. Pulsing can already be regarded as coding in the meaning of claim 6. Furthermore, an alternative solution to the problem of noise reduction can also be found in D5 (col. 10, l. 53 - col. 11, l. 3) where chirp pulses are used for encoding illumination light. Consequently, starting from the disclosure of D3 it would be obvious for the man skilled in the art to apply linear FM or chirp pulse coding as known from D5, thus arriving at a method having all features of claim 6.

4.4 Thus, claim 6 lacks an inventive step (Article 33(3) PCT).

5. Dependent claims 2 - 5 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, since they relate to slight constructional modifications of the device already known from D5 which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of claims 2 - 5

also lack an inventive step.

6. It is noted that the second alternative method for coding disclosed in claims 1 and 6, binary pulse coding or coding by random codewords, is known from D6 (p. 7, l. 8 - 16).

WE CLAIM

1. An optical system for detecting one or more optical responses of biological tissue, said optical system comprising:

(a) a photonic energy source for emitting electromagnetic radiation;

(b) an optical emission processing means for receiving the electromagnetic radiation from the photonic energy source and isolating one or more illumination wavelengths of the electromagnetic radiation, said optical emission processing means encoding the one or more illumination wavelengths using one or more pseudo random codewords or linear FM thereby generating an encoded signal, the optical emission processing means transmitting the encoded signal to the biological tissue;

(c) an optics assembly providing a means for aligning emitter optics of the optical emission processing means with detector optics of a received light optical processing means;

(d) a received light optical processing means for collecting and isolating one or more wavelengths of received electromagnetic radiation from the biological tissue created in response to the encoded signal and transmitting the one or more wavelengths of received electromagnetic radiation to an optical detector;

(e) an optical detector for sensing and converting the one or more wavelengths of received electromagnetic radiation into an electrical signal; and

(f) digital signal processing means for correlating the electrical signal received from the optical detector with the encoded signal thereby identifying an optical response of the biological tissue to the one or more illumination wavelengths, said digital signal processing means controlling the functionality of the photonic energy source, the optical emission processing means and the received light optical processing means.

2. The system for detecting optical characteristics of biological tissue according to claim 1, wherein the digital signal processing means is a circuit board which is integrated into a computing system.

3. The system for detecting optical characteristics of biological tissue according to claim 1, wherein the photonic energy source is selected from the group comprising a laser, a laser diode, a light emitting diode, an arc flashlamp or a continuous wave bulb.

4. The system for detecting optical characteristics of biological tissue according to claim 1, wherein optical emission processing means and the received light optical processing means include one or more optical devices selected from the group comprising condensers, focusing devices, lenses, fibre optics, apertures and monochromators.

5. The system for detecting optical characteristics of biological tissue according to claim 1, wherein the optical detector is selected from the group comprising a gallium-arsenide photodiode, a cadmium sulfide photodiode or a silicon avalanche diode.

6. Use of an optical system for generating a pattern of optical characteristics of biological tissue, said optical characteristics being reflectance and fluorescence characteristics of the illuminated biological tissue, said optical system comprising:

(a) a photonic energy source for emitting electromagnetic radiation;

(b) an optical emission processing means for receiving the electromagnetic radiation from the photonic energy source and isolating one or more illumination wavelengths of the electromagnetic radiation, said optical emission processing means encoding the one or more illumination wavelengths using one or more pseudo random codewords or linear FM thereby generating an encoded signal, the optical emission processing means transmitting the encoded signal to the biological tissue;

(c) an optics assembly providing a means for aligning emitter optics of the optical emission processing means with detector optics of a received light optical processing means;

(d) a received light optical processing means for collecting and isolating one or more wavelengths of received electromagnetic radiation from the

biological tissue created in response to the encoded signal and transmitting the one or more wavelengths of received electromagnetic radiation to an optical detector;

(e) an optical detector for sensing and converting the one or more wavelengths of received electromagnetic radiation into an electrical signal; and

(f) digital signal processing means for correlating the electrical signal received from the optical detector with the encoded signal thereby identifying an optical response of the biological tissue to the one or more illumination wavelengths, said digital signal processing means controlling the functionality of the photonic energy source, the optical emission processing means and the received light optical processing means.

7. A method for detecting one or more optical responses of biological tissue and creating a pattern of the one or more optical responses, said method comprising the steps of:

(a) generating one or more illumination wavelengths of electromagnetic radiation;

(b) encoding said one or more illumination wavelengths using one or more pseudo random codewords or linear FM thereby generating an encoded signal;

(c) illuminating the biological tissue with the encoded signal, in order to generate encoded reflectance and fluorescence from the biological tissue in response thereto;

(d) collecting said encoded reflectance and fluorescence;

(e) correlating said encoded reflectance and fluorescence with the encoded signal thereby identifying one or more optical responses to the one or more illumination wavelengths;

(f) repeating steps a) through e) for a next one or more wavelengths of electromagnetic radiation;

(g) generating a pattern of the one or more optical responses, said pattern being a representation of a particular one or more optical responses matched with a particular one or more illumination wavelengths.

8. The method for detecting one or more optical responses of biological tissue according to claim 7, wherein the pattern is a contour map, and a position on the contour map is represented by an illumination wavelength and a detection wavelength and intensity of the collected reflectance and fluorescence is represented by contours.

9. The method for detecting one or more optical responses of biological tissue according to claim 7, wherein the pattern is a comparative pattern between detected optical responses of two biological tissue samples, said comparative pattern identifying optical response differences between the two biological tissue samples.

10. The method for detecting one or more optical responses of biological tissue according to claim 7, wherein the pattern is a three dimensional representation of the collected reflectance and fluorescence.

11. The method for detecting one or more optical responses of biological tissue and creating a pattern of the one or more optical responses according to claim 7, wherein the optical characteristics of biomarkers within the biological tissue are determined.

12. The method for detecting one or more optical responses of biological tissue according to claim 7, further comprising the step of determining a statistical significance value related to each of the one or more optical responses, said statistical significance value representative of a ratio of signal-to-noise determined during detection.

13. The method for detecting one or more optical characteristics responses of biological tissue according to claim 7, wherein the pattern is a comparative pattern between detected optical responses of an identical location of the biological tissue sample detected at different points in time, said comparative pattern identifying optical response differences of the biological tissue sample over time.

14. The method for detecting one or more optical characteristics responses of biological tissue according to claim 7, wherein the pattern is a comparative pattern between detected optical responses of two or more different locations of the biological tissue sample, said comparative pattern identifying optical response differences of the two or more different locations of the biological tissue sample.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA 03/01372

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-37 as originally filed

Claims, Numbers

1-14 received on 15.10.2004 with letter of 15.10.2004

Drawings, Sheets

1/15-15/15 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-6 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-6
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations

see separate sheet